REMARKS

Applicants submit this Amendment in response to the Office Action mailed June 5, 2002. Claim 34 is pending in the application. Claims 35-42 are added, and find support in the specification at least as follows:

Claim 35: page 33, lines 10-27;

Claim 36: page 37, line 28 through page 38, line 4;

Claims 37-39, page 33, lines 18-23;

Claim 40, page 37, lines 22-27; and

Claims 41 and 42, page 21, lines 17-19; page 22, lines 17-19; and page 28, line 38 through page 38, line 4.

Such support is exemplary only, and includes reference to any figures mentioned therein.

With this Amendment claim 34 is amended to recite "mammal" instead of "animal." The amendment is supported at page 20, lines 4-5, which provides a variety of non-human mammals suitable as transgenic mammals.

The Examiner objected to the specification under 35 U.S.C. § 112, first paragraph, and rejected claim 34 as the specification allegedly is not enabling for any and all transgenic non-human animals whose cells express a transgene that contains a Fkh^{sf} coding sequence. Reconsideration and withdrawal of this rejection are respectfully requested. Applicants note that claim 34 has been amended to recite "transgenic non-human mammals."

A specification is presumed to be enabling and the U.S. Patent and Trademark Office (PTO) has the burden of establishing a *prima facie* case of lack of enablement. *See, In re Angstadt*, 190 U.S.P.Q. 214, 219 (C.C.P.A. 1976); *In re Marzocchi*, 169 U.S.P.Q. 367, 369-370 (C.C.P.A. 1971). To make a *prima facie* case of lack of enablement, the PTO must come forward with reasons, supported by the record as a whole, showing why the specification fails to enable one of ordinary skill in the art to make and use the claimed invention. *In re Angstadt*, 190 U.S.P.Q. 214, 219 (C.C.P.A. 1976). The mere fact that some experimentation is necessary does

not negate enablement as long as undue experimentation is not required. *See* M.P.E.P. § 608.01(p).

The burden is on the PTO to establish that experimentation would be undue, *Angstadt*, 190 U.S.P.Q. at 219, taking into consideration the eight factors that are to be considered in determining whether a disclosure requires undue experimentation. *In re Wands*, 8 U.S.P.Q.2d 1400, 1404 (Fed. Cir. 1988). Applicants submit that the amount of experimentation which may be required to practice the present invention does not rise to the level of being undue experimentation, as defined by the Court in *Wands*.

An important aspect of the Court's decision in *Wands* is its finding that the nature of the technology pertinent to the Wands invention (monoclonal antibody production) permitted a broad definition of the term "experiment." The Court found that an "experiment" in the monoclonal antibody art consisted of the entire attempt to make a monoclonal antibody against a particular antigen. As described by the Court, the process entailed, "immunizing animals, fusing lymphocytes from the immunized animals with myeloma cells to make hybridomas, cloning the hybridomas, and screening the antibodies produced by the hybridomas for the desired characteristics." 8 U.S.P.Q.2d at 1407. Thus, *Wands* supports the conclusion that in a complex field such as monoclonal antibody production, the entire attempt to achieve the desired result, from beginning to end, constitutes one experiment.

According to the Court, repetition of this whole experiment more than once does not constitute undue experimentation. As the Court indicated, practitioners in the art would be prepared to screen negative hybridomas in order to find a hybridoma making the desired antibody. 8 U.S.P.Q.2d at 1406. Thus, the fact that some aspects of the experiment as a whole will yield negative results does not mandate a finding that the amount of experimentation to achieve a positive result is undue.

Like the production of monoclonal antibodies, the production of transgenic mammals whose cells express a specific transgene may require some experimentation, but if viewed in the light of *Wands*, this experimentation, and the possibility of encountering negative results along the path to the positive results, is not undue. Furthermore, the present applicants provide extensive guidance to allow one of ordinary skill in the art to obtain the DNA that is

utilized in the practice of the invention, and have reduced to practice the production of a transgenic mice that clearly express the gene in an appropriate manner.

In reference to the state of the art, the Examiner stated that,

> Transgene efficiency is low, and range from 1% in farm animals (cattle, sheep, pigs) to 3% in laboratory animals like rabbits, mice and rats.

(Paper No. 7 at page 4, lines 6-7.)

Furthermore, according to the Examiner, a transgene introduced into one species may have different effects in another species. (Paper No. 7 at page 4, lines 14-16.)

Applicants disagree with the Examiner's conclusions, and submit that one of skill in the art can follow the teachings of the specification and construct a transgenic mammal using the polynucleotides disclosed, or other appropriate polynucleotides from different species. The resulting mammals would be tested for the phenotypic effect of transgene expression, also as described in detail in the specification and the examples. As the Examiner has pointed out, expression of the Fkh^{sf} transgene overcame the lymphoproliferative defect found in scurfy mice. Thus, objective tests are provided for determining if the transgene is expressed in the mammal. Such tests would not constitute "undue" experimentation within the scope of *Wands*. The Examiner cited success rates of 1-3% for a variety of non-human mammals. In *Wands*, a success rate of 2.8% was not considered by the Court to necessitate a finding of "undue experimentation."

> Even if we were to accept the PTO's 2.8% success rate, we would not be required to reach a conclusion of undue experimentation. Such a determination must be made in view of the circumstances of each case and cannot be made solely by reference to a particular numerical cutoff.

(*Wands* at page 1406, fn 29.)

Such reasoning by the Court also indicates that the Examiner's reliance on the "low" rage of transgene efficiency (1-3%) does not lead to a conclusion of undue experimentation in a complex field such as production of transgenic mammals.

Finally, as applicants have amended claim 34 to recite non-human mammals, the Examiner's concern regarding non-mammalian species, such as insects, fish, reptiles and birds, is moot, and any lack of success in such species is no longer relevant to a determination of enablement.

In view of the foregoing remarks, applicants submit that the Examiner has not met his burden of making a *prima facie* showing that undue experimentation is required in order to practice the invention as claimed. Reconsideration and withdrawal of this rejection are respectfully requested.

The Examiner objects to the present specification because this application fails to fully comply with the requirements of 37 CFR 1.821 through 1.825. The alleged basis for this objection is that sequences are not identified by sequence identifiers.

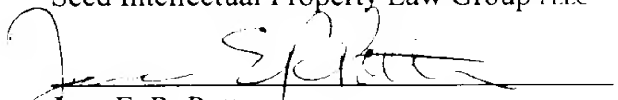
The examiner notes that the sequences in Figures 1-4 and at pages 34, 35 and 40 are not identified by SEQ ID NOS. This has been remedied by the amendment to the specification in the accompanying response to the Notice to Comply with the sequence rules.

Attached hereto is a marked-up version of the changes made to the specification and claims by the current amendment. The attached page is captioned "**Version With Markings to Show Changes Made**." Also attached is a copy of the pending claims with as of filing of this response.

All of the claims remaining in the application are now clearly allowable. Favorable consideration and a Notice of Allowance are earnestly solicited.

Respectfully submitted,

Seed Intellectual Property Law Group PLLC



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(JEP:cew) #294076

VERSION WITH MARKINGS TO SHOW CHANGES MADE

In the Claims:

Claim 34 has been amended as follows:

34. (Amended) A transgenic non-human [animal] mammal whose cells express a transgene that contains a sequence encoding Fkh^{sf} protein.

New claims 35-42 have been added.

(JEP:ccw) #294076

Pending Claims as of 07/17/02 [Amendment Under 1.111 Filing]
Application No. 09/696,867
[240083.501D6]

34. (Amended) A transgenic non-human mammal whose cells express a transgene that contains a sequence encoding Fkh^{sf} protein.

35. (New) A transgenic mouse whose cells express an exogenous transgene that contains a sequence encoding Fkh^{sf} protein.

36. (New) The transgenic mouse of claim 35, wherein the expression of said exogenous Fkh^{sf} transgene results in reduction of T-Lymphocyte proliferation in said mouse.

37. (New) The transgenic mouse of claim 35, wherein the expression of said exogenous Fkh^{sf} transgene results in normal size of said mouse.

38. (New) The transgenic mouse of claim 35, wherein the expression of said exogenous Fkh^{sf} transgene results in normal weight of said mouse.

39. (New) The transgenic mouse of claim 35, wherein the expression of said exogenous Fkh^{sf} transgene results in normal skin appearance of said mouse.

40. (New) The transgenic mouse of claim 35, wherein the expression of said exogenous Fkh^{sf} transgene results in a reduction of T-Lymphocytes.

41. (New) The transgenic mouse of claim 35, wherein the expression of said exogenous Fkh^{sf} transgene results in reduction in T-Lymphocyte responsiveness to cytokines.

42. (New) The transgenic mouse of claim 35, wherein the expression of said exogenous Fkh^{sf} transgene results in reduction in T-Lymphocyte sensitivity to stimulation through cell surface receptors.